REMARKS

Claims 1-82 are currently pending in the above-identified patent application. Claims 1-10, 13-30, 34-49, 52-60, and 62-82 have been withdrawn from consideration due to a Restriction Requirement that has been made final. Accordingly, claims 11-12, 31-33, 50-51, and 61 remain under consideration in the above-identified patent application.

Claims 11-12, 31-33, 50-51, and 61 were rejected under the second paragraph of 35 U.S.C. §112 as indefinite for being incomplete. The Examiner stated that the claims omitted essential structural cooperative relationships of elements.

Claims 11-12, 31-33, 50-51, and 61 were rejected under 35 U.S.C. § 102(b) as anticipated by, or, in the alternative, under 35 U.S.C. § 103(a) as obvious over each of U.S. Patent No. 5,532,137 to Niwa et al. ("Niwa et al. '137"), U.S. Patent No. 5,635,406 to Grenier et al. ("Grenier et al. '406"), PCT Publication No. WO 94/04700 to Fujisawa Pharmaceutical Co. ("Fujisawa (PCT)"), H.J. Jeong et al., "A New Monoclonal Antibody for the Immunosuppressive Drug Tacrolimus," Ther. Drug Monit. 21: 444 (1999) (Abstracts: 6th International Congress of TDM-CT) ("Jeong et al. (1999)"), or L. Bäckman et al., "FK506 Trough Levels in Whole Blood and Plasma in Liver Transplant Recipients," Transplantation 57: 519-525 (1994) ("Bäckman et al. (1994)").

Reexamination of the application as amended, reconsideration of the rejection and objections, and allowance of the claims are respectfully requested.

The period for response to this Office Action has been extended to June 17, 2001 by filing of a two-month Request for Extension of Time under 37 C.F.R. § 1.136(a) and payment of the appropriate fee. Accordingly, this Response is being filed in a timely manner.

I. AMENDMENTS TO THE APPLICATION

Entry of the amendments to the application is respectfully requested. As detailed below, the amendments introduce no new matter.

Claim 11 is amended as suggested by the Examiner to recite that the monoclonal antibody is produced by a hybridoma produced by the specified steps. Claim 11 is also amended to recite the properties of the monoclonal antibody originally recited in claim 1, now withdrawn from consideration. Therefore, these limitations do not introduce any new matter.

For the convenience of the Examiner and in compliance with recently-amended 37 C.F.R. § 1.121, Applicant has attached as a separate sheet a marked-up copy of the amendments, showing all changes relative to the previous version of the amended claim, claim 11, with the additions identified by underlining.

II. THE REJECTIONS UNDER THE SECOND PARAGRAPH OF 35 U.S.C. § 112

Claims 11-12, 31-33, 50-51, and 61 were rejected under the second paragraph of 35 U.S.C. §112 as indefinite. Specifically, it was stated that these claims were incomplete for omitting essential structural cooperative relationships of elements. This omission was stated to amount to a gap between the necessary structural connections.

The Examiner stated that this rejection could be overcome by inserting, in line 1 of claim 11, after the word "by", the phrase –a hybridoma produced by--. This amendment has been made to claim 11.

Accordingly, the Examiner is respectfully requested to withdraw this rejection.

III. THE § 102(b)/§ 103(a) REJECTIONS

Claims 11-12, 31-33, 50-51, and 61 were rejected under 35 U.S.C. § 102(b) as anticipated by, or, in the alternative, under 35 U.S.C. § 103(a) as obvious over each of U.S. Patent No. 5,532,137 to Niwa et al. ("Niwa et al. '137"), U.S. Patent No. 5,635,406 to Grenier et al. ("Grenier et al. '406"), PCT Publication No. WO 94/04700 to Fujisawa Pharmaceutical Co. ("Fujisawa (PCT)"), H.J. Jeong et al., "A New Monoclonal Antibody for the Immunosuppressive Drug Tacrolimus," Ther. Drug Monit. 21: 444 (1999) (Abstracts: 6th International Congress of TDM-CT) ("Jeong et al. (1999)"), or L. Bäckman et al., "FK506 Trough Levels in Whole Blood and Plasma in Liver Transplant Recipients," Transplantation 57: 519-525 (1994) ("Bäckman et al. (1994)").

This rejection is respectfully traversed.

As detailed below, the rejection over Jeong et al. (1999) is traversed on the grounds that the information recited in Jeong et al. (1999) is attributable to the inventors of the present application. Jeong et al. (1999) is an inventor-coauthored publication. Applicant shall submit a declaration under the holding of In re Katz, 215 U.S.P.Q. 14 (C.C.P.A. 1982). This declaration provides evidence that the article is describing the work of the applicants. Accordingly, there is no basis for the application of Jeong et al. (1999) as a reference in light of this showing.

With respect to the remaining references, these references do not teach or suggest the properties of the claimed invention. Namely, these references do not teach the binding affinity of the antibody for tacrolimus of about 3.7×10^9 liters/mole recited in claim 11. These references also do not teach the limited cross-reactivity of less than about 8% to all of the following tacrolimus metabolites: 15-demethyl tacrolimus; 31-demethyl tacrolimus; 13, 31-didemethyl tacrolimus; 15, 31-didemethyl tacrolimus; and 12-hydroxy tacrolimus as recited in claim 11.

Of these references, Niwa et al. '137 reports neither binding affinity nor lack of cross-reactivity to tacrolimus metabolites for the monoclonal antibodies described therein. There is no basis for assuming that the antibodies of Niwa et al. '137 share these properties with the antibody of claim 11 of the present application, especially in light of the fact that other antibodies tested in Example 6 of the present application exhibit cross-reactivity to tacrolimus metabolites greater than the 8% cutoff value recited in this claim.

Similarly, Grenier et al. '406 uses a binding protein to tacrolimus to stabilize the drug in an aqueous matrix and does not report either the binding affinity or the lack of cross-reactivity to tacrolimus metabolites for the monoclonal antibodies used in this method. These properties are irrelevant to the method of Grenier et al. '406.

Along the same lines, Fujisawa (PCT) does not even disclose an anti-FK506 antibody. Fujisawa (PCT) discloses a monoclonal antibody that binds not FK506 (tacrolimus), but a FK506 binding protein (FKBP). There is absolutely no teaching or suggestion in Fujisawa (PCT) that the monoclonal antibody disclosed therein would bind FK506 at all, much less that this antibody would have the desired properties of affinity and lack of cross-reactivity to tacrolimus metabolites recited in claim 11.

Finally, Bäckman et al. (1994) used monoclonal antibodies provided by Fujisawa (Bäckman et al. (1994), p. 521, 1st column, lines 10-11). There is no suggestion or teaching in Bäckman et al. (1994) that this antibody, which is most likely that of Niwa '137, has the required properties. Bäckman et al. (1994) does not recite either the binding affinity nor the lack of cross-reactivity of the antibody used. There is no reason to believe that these antibodies meet the limitations of claim 11 as amended, especially in light of the results of Example 6 of the present application.

In light of the amendment of claim 11 and these arguments, there is no basis for stating that claim 11 has a "specificity for tacrolimus which appears to be the same as or functionally equivalent to the monoclonal antibodies described in the prior art." The lack of cross-reactivity of the antibody of claim 11 sets it apart from the antibodies of the prior art. A rejection alternatively under § 102 for anticipation or § 103 for obviousness is proper only when the prior art discloses a product that "reasonably appears to be identical with or only slightly different than a product claimed." In re Brown, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972) (as applied to product claims in product-by-process form). The specific affinity of the antibody as now recited in claim 11 and the lack of reactivity with a number of tacrolimus metabolites means that this antibody cannot be "identical with or only slightly different than" prior art antibodies. These are significant differences and affect the activity and use of the antibodies.

With respect to the comments made by the Examiner in the first full paragraph of page 5 of the Office Action, the carbon-22-substituted immunogen of Example 2 was in fact used to prepare the antibody of claim 11. The antibody 14H04 of Example 6 resulted from the same cloning procedure of Example 5 used to produce the antibody of claim 11 but was from another clone.

If a claim to the antibody is neither anticipated nor obvious, then claims to immunoassays (claim 50) or test kits (claim 61) can be neither anticipated nor obvious.

Accordingly, the Examiner is respectfully requested to withdraw the rejection as applied to the amended claims.

IV. CONCLUSION

In conclusion, all claims under consideration are allowable. These claims particularly point out and distinctly claim that which Applicants regard as their invention. Additionally, these claims are neither anticipated by nor obvious over the references of record. Accordingly, prompt allowance of these claims is respectfully requested.

Respectfully submitted,

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Marc P. Bobys
Registration No. 45,267

OPPENHEIMER WOLFF & DONNELLY LLP
2029 Century Park East, 38th Floor
Los Angeles, California 90067-3024
Phone: (310) 788-5000
Fax: (310) 788-5100

Attachment: Declaration of Dr. Kenneth C. Kasper Under 37 C.F.R. 1.132

MARKED UP AMENDED CLAIMS

Claim 11 is amended as follows:

11. (Once amended) A monoclonal antibody to tacrolimus produced by a hybridoma produced by fusion of antibody-producing cells from an antibody-producing mammal immunized with tacrolimus derivatized with a carboxymethyl oxime moiety at carbon atom 22 conjugated to a high molecular weight protein with a suitable fusion partner, that has a binding affinity for tacrolimus of about 3.7×10^9 liters/mole, that cross-reacts with 13-demethyl tacrolimus, and that has less than about 8% cross-reactivity to all of the following tacrolimus metabolites: 15-demethyl tacrolimus; 31-demethyl tacrolimus; 13,31-didemethyl tacrolimus; 15,31-didemethyl tacrolimus; and 12-hydroxy tacrolimus.